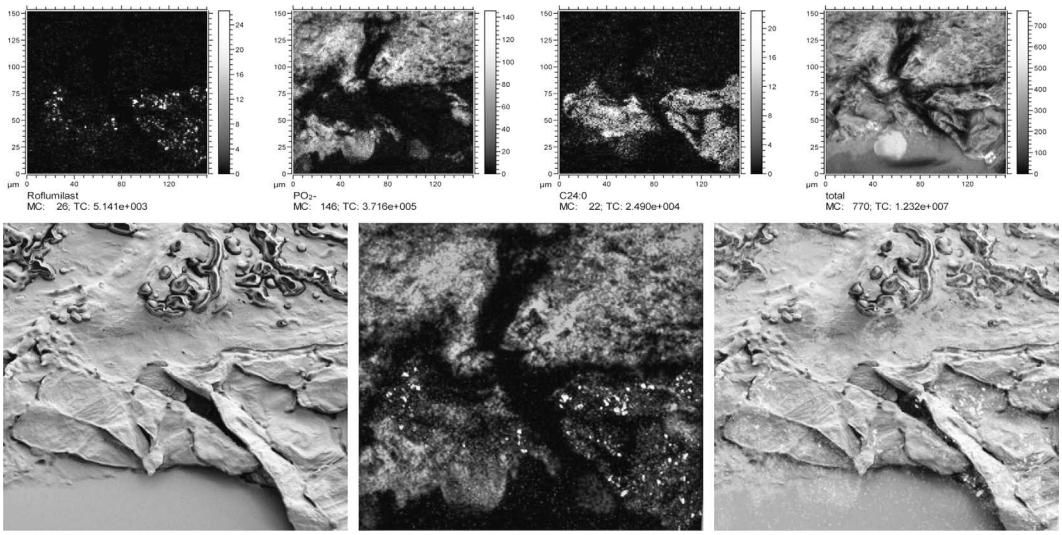

FIGURE 56.13 High-resolution TOF-SIMS images (top panels) and SEM images (bottom panels) showing the distribution of roflumilast in the stratum corneum of a roflumilast-treated mouse ear. Field of view is 150 × 150 μm^2. In overlay images, roflumilast is shown in green, lipid is red, and cholesterol is blue. (Reprinted with permission from Siovall et al. 2014.)

biopsy of the sample using a blade. The combination of TOF-SIMS and SEM was beneficial to study drug distribution and penetration.

56.8 OPTICAL COHERENT TOMOGRAPY

Optical coherence tomography (OCT) is a noninvasive, label-free optical imaging approach that detects scattered near-infrared (NIR) laser light signals from tissue, which predominantly avoids disruption of the skin tissue. Optical imaging tools such as reflectance microscopy (described later in this chapter) and OCT can provide a real-time "optical biopsy" in clinics. It is useful to detect early stage skin cancer by visualization of target tissue morphology with micrometer resolution in real time. NIR dyes and microparticles and nanoparticles have been explored as OCT contrast agents.

Kim et al. (2009) hypothesized that gold nanoparticles (AuNPs) would be a good candidate for an OCT contrast agent, as well as delivering biological molecules [24]. AuNPs are biocompatible, easy to synthesize, and can be functionalized with additional modalities. The aim of this study was to improve the penetration and distribution of AuNPs using microneedles and ultrasound and therefore enhance contrast in vivo OCT images of oral dysplasia in a hamster model. One side of the cheek pouch of a hamster was treated topically with 0.5% (v/v) 9,10-dimethyl-1,2-benzanthracene (DMBA) three times a week for five months to induce cancer. AuNPs were conjugated with monoclonal antibodies binding to epidermal growth factor, which is overexpressed in oral cancer. The check pouch was attached to a microscope using a custom-built clamp to fasten it to the stage. Microneedles were applied to the pouch and then AuNPs solution was applied to the site for 10 minutes. Ultrasound was then applied to the same spot for one minute to improve nanoparticle delivery. OCT images (Figure 56.14) show AuNPs penetrated deeper into the tissue when microneedles were applied. There was a visible difference between carcinogen-treated and untreated tissue. Ultrasound seems to distribute AuNPs more homogenously on the surface of the skin. When they took an enlarged image of dysplasia (Figure 56.14, bottom) and used scion image analysis software for data processing, considerably greater light scattering in the stratum corneum and upper epithelial layers